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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/507,479	09/13/2004	Jean-Yves Reginster	P70090US0	6747

136 7590 10/06/2006

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EXAMINER	
FOSTER, CHRISTINE E	

ART UNIT	PAPER NUMBER
1641	

DATE MAILED: 10/06/2006

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	10/507,479	REGINSTER ET AL.	
	Examiner	Art Unit	
	Christine Foster	1641	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 1 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *27 June 2006*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-26* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☐ Claim(s) _____ is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☒ Claim(s) *1-26* are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☒ Other: *Notice to Comply*.

DETAILED ACTION

Election/Restrictions

1. Restriction is required under 35 U.S.C. 121 and 372.

This application contains the following inventions or groups of inventions which are not so linked as to form a single general inventive concept under PCT Rule 13.1.

In accordance with 37 CFR 1.499, applicant is required, in reply to this action, to elect a single invention to which the claims must be restricted.

Group I, claim(s) 1-10, drawn to a method for performing an assay for protein oxidation.

Group II, claim(s) 11-17, drawn to an immunological binding partner and a cell line producing a monoclonal antibody.

Group III, claim(s) 18-22, drawn to a method for investigating the existence of extent of a pathological state.

Group IV, claim(s) 23-26, drawn to a kit for use in performing the method of claim 1.

2. The inventions listed as Groups I-IV above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, they lack the same or corresponding special technical features for the following reasons:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. The inventions listed as Groups I-IV do not relate to a single general inventive concept because they lack the same or corresponding special technical feature.

The technical feature linking Groups I-IV relates to the detection of protein oxidation by detecting an amino acid sequence characteristic of a specific protein that contains an aromatic amino acid residue in nitrated form.

However, Paik et al. (Connective Tissue Research Vol. 4212, p. 111-122; Applicant's IDS of 1/13/05) teach detection of nitrotyrosine-containing collagen (see in particular the abstract; p. 115, "Detection of 3-nitro-tyrosine"; and p. 120).

Regarding the feature of an immunological binding partner specifically reactive with the nitrated form of an amino acid residue as in Groups II and IV, this feature is shown by Beckman et al. (WO 96/04311) to lack novelty as Beckman et al. teach monoclonal antibodies that recognize amino acid sequences containing nitrotyrosine (the abstract). For example, Beckman et al. teach the detection of nitric oxide synthase that contains nitrotyrosine (p. 23-24 in particular).

Therefore, the technical feature(s) linking the inventions of Groups I-IV does not constitute a special technical feature as defined by PCT Rule 13.2, as it does not define a contribution over the prior art.

In addition, Groups I-IV each have technical features that are unrelated to the other groups. Group I includes the feature of an assay for protein oxidation, which is not a feature of Groups II-III. Group II includes the feature of an immunological binding partner, which is not a requirement of the independent claims of Groups I or III. Group III includes the feature of investigating the existence or extent of a pathological state, which is not a feature of the other Groups. Group IV includes the feature of a means for detecting binding, which is not a limitation of the other Groups.

Accordingly, Groups I-IV are not linked by the same or a corresponding special technical feature so as to form a single general inventive concept.

Election of Species

3. This application contains claims directed to more than one species of the generic invention. These species are deemed to lack unity of invention because they are not so linked as to form a single general inventive concept under PCT Rule 13.1.

The species are as follows:

a. **An amino acid sequence which is characteristic of a specific protein.**

A specific sequence must be specified; see claims 9-10, 12, and 13-15.

In the event that Group III is elected, the following species election must also be made:

b. **Pathological state (elect one of the following):**

i. Oxidative damage associated with an inflammatory joint disease (a specific inflammatory joint disease must be specified); see claim 19

ii. Cancer (see claim 20)

iii. Alzheimer's disease (see claim 20)

iv. Parkinson's disease (see claim 20)

v. An inflammatory bowel disease (a specific inflammatory joint disease must be specified); see claim 20

vi. Systemic lupus erythematosus (see claim 20)

vii. Osteoarthritis (see claim 20)

viii. Rheumatoid arthritis (see claim 20)

Applicant is required, in reply to this action, to elect a single species to which the claims shall be restricted if no generic claim is finally held to be allowable. **The reply must also identify the claims readable on the elected species, including any claims subsequently**

added. An argument that a claim is allowable or that all claims are generic is considered non-responsive unless accompanied by an election.

Upon the allowance of a generic claim, applicant will be entitled to consideration of claims to additional species which are written in dependent form or otherwise include all the limitations of an allowed generic claim as provided by 37 CFR 1.141. If claims are added after the election, applicant must indicate which are readable upon the elected species. MPEP § 809.02(a).

4. The claims are deemed to correspond to the species listed above in the following manner: The following claim(s) are generic: claims 1-4, 11, 16-17, and 23-26. Claims 5-10, 12-15, 18-22 are subject to species election.

5. The species listed above do not relate to a single general inventive concept under PCT Rule 13.1 because, under PCT Rule 13.2, the species lack the same or corresponding special technical features for the following reasons: the species of **amino acid sequences** are different because:

According to PCT Rule 13.2, unity of invention exists only when the shared same or corresponding technical feature is a contribution over the prior art. According to the guidelines in Section (f)(i)(B)(l) of Annex B of the PCT Administrative Instructions, all alternatives of a Markush Group have a common structure. Although the various amino acid sequences representative of different proteins share a common structure of a nitrated aromatic amino acid residue, the sequences are not regarded as being of a similar nature because the shared common structure is not a contribution over the prior art, as Beckman et al. teach detection of amino acid sequences containing nitrotyrosine. Therefore, the feature of a nitrated aromatic amino acid

residue cannot be considered to be a special technical feature as it does not make a contribution over the prior art.

The species of **pathological states** are different because the pathological conditions differ in etiologies, symptoms, course of disease, treatments, and therapeutic endpoints; thus each condition represents patentably distinct subject matter. Furthermore, the technical feature shared by these various pathological states as claimed relates to the detection of an amino acid sequence which contains one or more aromatic amino acids in nitrated form for diagnosis of disease. However, this feature is shown by Beckman et al. (discussed above) to lack novelty (see the title and abstract). Therefore, the feature of pathological state or disease cannot be considered to be a special technical feature as it does not make a contribution over the prior art.

Applicant is advised that the reply to this requirement to be complete must include (i) an election of a species or invention to be examined even though the requirement be traversed (37 CFR 1.143) and (ii) identification of the claims encompassing the elected invention.

The election of an invention or species may be made with or without traverse. To reserve a right to petition, the election must be made with traverse. If the reply does not distinctly and specifically point out supposed errors in the restriction requirement, the election shall be treated as an election without traverse.

Should applicant traverse on the ground that the inventions or species are not patentably distinct, applicant should submit evidence or identify such evidence now of record showing the inventions or species to be obvious variants or clearly admit on the record that this is the case. In either instance, if the examiner finds one of the inventions unpatentable over the prior art, the evidence or admission may be used in a rejection under 35 U.S.C.103(a) of the other invention.

6. Applicant is reminded that upon the cancellation of claims to a non-elected invention, the inventorship must be amended in compliance with 37 CFR 1.48(b) if one or more of the currently named inventors is no longer an inventor of at least one claim remaining in the application. Any amendment of inventorship must be accompanied by a request under 37 CFR 1.48(b) and by the fee required under 37 CFR 1.17(i).

Notice of Possible Rejoinder

The examiner has required restriction between product and process claims. Where applicant elects claims directed to the product, and the product claims are subsequently found allowable, withdrawn process claims that depend from or otherwise require all the limitations of the allowable product claim will be considered for rejoinder. All claims directed a nonelected process invention must require all the limitations of an allowable product claim for that process invention to be rejoined.

In the event of rejoinder, the requirement for restriction between the product claims and the rejoined process claims will be withdrawn, and the rejoined process claims will be fully examined for patentability in accordance with 37 CFR 1.104. Thus, to be allowable, the rejoined claims must meet all criteria for patentability including the requirements of 35 U.S.C. 101, 102, 103 and 112. Until all claims to the elected product are found allowable, an otherwise proper restriction requirement between product claims and process claims may be maintained. Withdrawn process claims that are not commensurate in scope with an allowable product claim will not be rejoined. See MPEP § 821.04(b). Additionally, in order to retain the right to rejoinder in accordance with the above policy, applicant is advised that the process claims should be amended during prosecution to require the limitations of the

product claims. Failure to do so may result in a loss of the right to rejoinder. Further, note that the prohibition against double patenting rejections of 35 U.S.C. 121 does not apply where the restriction requirement is withdrawn by the examiner before the patent issues. See MPEP § 804.01.

The Examiner notes that the instant application is a national stage entry of PCT/EP03/02559 filed under 35 U.S.C. § 371. For purposes of restriction, lack of unity practice has been applied to the pending claims under 35 U.S.C. § 121 and 372. Lack of unity will be reassessed at each stage of prosecution hereafter.

Conclusion

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Christine Foster whose telephone number is (571) 272-8786. The examiner can normally be reached on M-F 8:30-5. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Long Le can be reached on (571) 272-0823. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

Christine Foster, Ph.D.
Patent Examiner
Art Unit 1641

LONG V. LE 09/29/06
SUPERVISORY PATENT EXAMINER
TECHNOLOGY CENTER 1600

NOTICE TO COMPLY WITH REQUIREMENTS FOR PATENT APPLICATIONS CONTAINING NUCLEOTIDE SEQUENCE AND/OR AMINO ACID SEQUENCE DISCLOSURES

Applicant must file the items indicated below within the time period set the Office action to which the Notice is attached to avoid abandonment under 35 U.S.C. § 133 (extensions of time may be obtained under the provisions of 37 CFR 1.136(a)).

The nucleotide and/or amino acid sequence disclosure contained in this application does not comply with the requirements for such a disclosure as set forth in 37 C.F.R. 1.821 - 1.825 for the following reason(s):

☐ 1. This application clearly fails to comply with the requirements of 37 C.F.R. 1.821-1.825. Applicant's attention is directed to the final rulemaking notice published at 55 FR 18230 (May 1, 1990), and 1114 OG 29 (May 15, 1990). If the effective filing date is on or after July 1, 1998, see the final rulemaking notice published at 63 FR 29620 (June 1, 1998) and 1211 OG 82 (June 23, 1998).

☐ 2. This application does not contain, as a separate part of the disclosure on paper copy, a "Sequence Listing" as required by 37 C.F.R. 1.821(c).

☐ 3. A copy of the "Sequence Listing" in computer readable form has not been submitted as required by 37 C.F.R. 1.821(e).

☒ 4. A copy of the "Sequence Listing" in computer readable form has been submitted. However, the content of the computer readable form does not comply with the requirements of 37 C.F.R. 1.822 and/or 1.823, as indicated on the attached copy of the marked -up "Raw Sequence Listing."

☐ 5. The computer readable form that has been filed with this application has been found to be damaged and/or unreadable as indicated on the attached CRF Diskette Problem Report. A Substitute computer readable form must be submitted as required by 37 C.F.R. 1.825(d).

☐ 6. The paper copy of the "Sequence Listing" is not the same as the computer readable from of the "Sequence Listing" as required by 37 C.F.R. 1.821(e).

☒ 7. Other: The specification includes amino acid sequences greater than 4 amino acids that are not accompanied by SEQ ID NOs. See page 17, lines 6-7, 12-13, and 18-19; page 19, line 4; page 20, lines 14-15 and 17; page 21, lines 4-5, 6-7, 10-11, and 18-20; page 22, lines 9-10, 23, and line 31 (which ends at p. 23, line 1); page 23, lines 4-5; page 29, line 23; and claims 12-15.
In addition, the sequence listing and computer readable form (CRF) submitted by Applicant are not in compliance because the same SEQ ID NO has been used to designate different amino acid sequences: see Applicant's response at p. 4, in reference to the specification replacement paragraph starting at page 19, line 4, in which "SEQ ID NO:1" has been used to designate both a nitrosylated peptide and a non-nitrosylated peptide.

Applicant Must Provide:

☒ An initial or substitute computer readable form (CRF) copy of the "Sequence Listing".

☒ An initial or substitute paper copy of the "Sequence Listing", **as well as an amendment specifically directing its entry into the application**.

☒ A statement that the content of the paper and computer readable copies are the same and, where applicable, include no new matter, as required by 37 C.F.R. 1.821(e) or 1.821(f) or 1.821(g) or 1.825(b) or 1.825(d).

For questions regarding compliance to these requirements, please contact:

For Rules Interpretation, call (703) 308-4216 or (703) 308-2923
For CRF Submission Help, call (703) 308-4212 or 308-2923
PatentIn Software Program Support
Technical Assistance.....703-287-0200
To Purchase PatentIn Software.....703-306-2600

PLEASE RETURN A COPY OF THIS NOTICE WITH YOUR REPLY

IFWO

RAW SEQUENCE LISTING DATE: 07/03/2006
PATENT APPLICATION: US/10/507,479 TIME: 12:24:43

Input Set : A:\Sequence Listing.txt
Output Set: N:\CRF4\07032006\J507479.raw

```
 3 <110> APPLICANT: Reginster, Jean-Yves
 4       Deberg, Michele
 5       Henrotin, Yves
 6       Christgau, Stephan
 8 <120> TITLE OF INVENTION: Detection of Specific Nitrated Protein Markers
10 <130> FILE REFERENCE: P70090US0
12 <140> CURRENT APPLICATION NUMBER: US 10/507,479
14 <141> CURRENT FILING DATE: 2004-09-13
16 <150> PRIOR APPLICATION NUMBER: PCT/EP03/02559
18 <151> PRIOR FILING DATE: 2003-03-12
20 <160> NUMBER OF SEQ ID NOS: 2
22 <170> SOFTWARE: PatentIn version 3.2
24 <210> SEQ ID NO: 1
25 <211> LENGTH: 9
26 <212> TYPE: PRT
27 <213> ORGANISM: Artificial sequence
29 <220> FEATURE:
30 <223> OTHER INFORMATION: Synthesized
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34 His Arg Gly Tyr Pro Gly Leu Asp Gly
35 1               5
37 <210> SEQ ID NO: 2
38 <211> LENGTH: 6
39 <212> TYPE: PRT
40 <213> ORGANISM: Artificial sequence
42 <220> FEATURE:
43 <223> OTHER INFORMATION: Synthesized
45 <400> SEQUENCE: 2
47 Leu Gln Tyr Met Arg Ala
48 1               5
```

SEQ ID NO:1 has been used to designate both unmodified peptides having this sequence as well as peptides containing the modified amino acid nitrotyrosine, which is incorrect.

The sequence(s) including nitrotyrosine must be presented as such and must be assigned a different SEQ ID NO.